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Urinary tract infections in patients with malignant neoplasms of the genitourinary system

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Summary

Aim

To diagnose the etiological factors involved in urinary tract infections (UTI) and to examine antibiotic sensitivities in bacteria – causative agents of UTI in female patients with genitourinary malignancies.

Materials/Methods

Nineteen patients aged between 35 and 75 years treated for genitourinary malignancies and with a diagnosis of UTI were examined. The majority of these patients (17) were treated with X rays to the pelvic region (tele – and brachytherapy). Six patients were treated for endometrial carcinoma. One patient was treated for ovarian cancer, and one for vaginal cancer. Significant bacteriuria was defined as 10^4 or more CFUs/ml in quantitative urine examination. Microorganisms were identified according to standard bacteriological methods using bio-Merieux tests. The isolated bacteria were tested for antibiotic sensitivity using the ATB Expression system.

Results

E. coli was the most frequently observed causative factor in cases of UTI. *E. faecalis* strains were the next most commonly observed species. One of 11 isolated *E. coli* strains was resistant to 5 antibiotics, a second was resistant to 3 antibiotics and three strains were resistant to 2 antibiotics. *E. coli* strains were classified into 9, and *E. faecalis* into 4, sensitivity patterns. UTI was diagnosed in four patients with stage I B, in four with stage III B and in one patient with stage IV cervical cancer.

Conclusions

E. coli and *E. faecalis* were the most frequently isolated species from the urine of female patients with genitourinary malignancies. These bacteria are among the main causative agents of UTI. The results of these investigations may be used for epidemiological purposes: to find the causes and sources of nosocomial infections and in the prophylaxis of these infections.

Key words **urinary tract infections • genitourinary cancers**

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Background

Urinary tract infections (UTI) are very often observed and occur more frequently in women than in men [1,2]. Infection in women is more frequent because of the close proximity of the reproductive and lower urinary tracts. Among factors increasing the risk of UTI are diabetes, vaginal inflammation, disorders of the reproductive organs and urinary bladder, neoplastic diseases and invasive gynaecological surgery [3,4]. Patients with malignant neoplasms of the genitals often suffer simultaneously from inflammation of the uterus and vagina. Patients who have undergone surgery (for cancer or for other reasons) may suffer infection of the urinary tract as a complication of the surgery, catheterisation or cystoscopy [5]. Radiotherapy, which used alongside surgery is a standard method in the treatment of these tumours, may also be a factor increasing the risk of UTI as it causes inflammatory changes to the epithelium of the urinary bladder [6].

General factors in the etiology of UTI are *E. coli* and other organisms of the family *Enterobacteriaceae* and *Enterococcus spp.* [7–9]. UTI may arise as a nosocomial infection and this is the most frequently observed form of this infection [10–12]. In epidemiological studies, aimed at finding the sources of nosocomial infections, it is important to identify the bacterial species involved. One of the methods used to differentiate bacterial species is to determine their sensitivity to drugs. Obviously the basic purpose of an antibiogram is to determine effective antibacterial medication to facilitate efficient treatment of the UTI. Because various species are resistant to treatment, for example *E. coli* which can be resistant to trimethoprim-sulfamethoxazole (standard treatment for UTI), antibiograms are required to identify other medicines [13]. Urinary tract infections (UTI) are among the factors increasing mortality and prolonged stays in hospital [14,15]. One symptom of UTI is the occurrence of symptomatic bacteriuria in which a count of 10^4 to 10^5 CFUs/ml (colony forming units/ml) is the threshold value [5,10,16].

Nonetheless, the majority of papers published on the subject of urinary tract disorders including inflammation are on patients with cancers of the uterine cervix [17–20] and few authors give any special value to UTI as a post therapeutic complication after radiotherapy on malignant neoplasms of the reproductive system in women [5,6]. Correct etiological diagnosis and appropriate treatment can have the effect of reducing the numbers of nosocomial infections.

Aim

The purpose of this study was to diagnose the etiological factors in urinary tract infection and to determine the drug sensitivities of bacteria causing UTI in patients with malignant neoplasms of the reproductive system. A further purpose for the study was to use information gained about drug sensitivities of the organisms.

Materials and Methods

We investigated 19 patients, aged between 35 and 75 years, being treated for malignant neoplasms of the urinary tract in the Department of Radiotherapy and Gynaecological Oncology at the Great Poland Cancer Centre and diagnosed as having symptomatic bacteriuria. The group included 17 patients being treated for tumours of the genitalia, one patient with cancer of the urethra and one with cancer of the urinary bladder. The largest group was patients treated for cancer of the uterine cervix – 9 patients – 5 of whom had undergone previous surgery. Six patients suffered from endometrial cancer, 5 of whom underwent surgical treatment. One patient was treated for ovarian cancer and one for cancer of the vagina.

Table 1. Etiological factors of UTI in patients with genitourinary malignancies.

Test Number	Age (years)	Results of Urine Culture
1	45	*P. mirabilis, S. equisimilis*
2	35	*E. faecalis, E. coli*
3	68	*E. coli*
4	47	*K. pneumoniae*
5	70	*P. aeruginosa*
6	69	*E. coli*
7	47	*E. coli*
8	65	*E. coli*
9	47	*E. faecalis, P. aeruginosa*
10	67	*S. agalactiae*
11	68	*E. faecalis*
12	67	*E. coli*
13	47	*E. coli, E. faecalis*
14	54	*E. coli*
15	70	*E. cloacae*
16	75	*E. coli*
17	58	*P. mirabilis, P. aeruginosa, K. oxytoca*
18	48	*E. faecalis, E. coli*
19	62	*E. coli*

In the cases of 12 patients this was their first operation. In this group of patients, throughout the time of surgery, urine was taken from the bladder via urethral catheter. The next 5 patients were catheterised during radiotherapy. The majority, 17 patients, were treated with ionising radiation to the pelvic region (tele and brachytherapy).

In all cases, clinical findings agreed with histopathological findings. The group of women suffering from invasive intraepithelial neoplasia of the cervix were in stages I B, III B and IV of tumour advancement.

Bacteriuria was defined as 10^4 and higher CFUs/ml of urine tested in quantitative tests. Qualitative and quantitative analysis of urine included CPS, D-Coccosel, Cetrimide, Albicans ID2 using quantitative loops. All 'under bed' tests were pro-

Table 2. Sensitivity Patterns of *E. coli.*

Pattern Number	Patient Number	Pattern									
		AMC	CFT	CTX	CAZ	AKN	GEN	NET	NOR	CIP	TSU
1	2,19	2	2	2	2	2	2	2	2	2	2
2	3	2	2	2	2	2	2	2	2	0	0
3	6	1	0	0	2	2	2	2	2	2	2
4	7	2	0	2	2	0	2	2	2	2	2
5	8,12	1	1	2	2	2	2	2	2	2	2
6	13	2	0	0	0	2	2	2	2	2	2
7	14	2	1	2	2	2	2	2	2	2	2
8	16	1	2	2	2	2	2	2	2	2	2
9	18	2	0	2	2	2	0	0	2	0	0

2 – Sensitive; 1 – Mildly Sensitive; 0 – Resistant.
AMC – amoxicillin/clarulanic acid; GEN – gentamicin; CFT – cefalotine; NET – netylmicin; CTX – Cefotaxime; NOR – Norfloxacin; CAZ – Ceftazidime; CIP – Ciprofloxacin; AKN – Amikacin; TSU – Cotrimoxazole.

Table 3. Sensitivity patterns of *E. faecalis.*

Pattern Number	Patient Number	Pattern									
		PIC	TET	ERY	CIP	VAN	TEC	GEN	KAN	AMP	PE
1	2,9	2	0	0	0	2	2	0	2	2	2
2	11	2	0	0	0	2	2	1	2	2	2
3	13	2	0	0	0	2	2	2	2	2	2
4	18	2	0	1	2	2	2	0	2	2	2

2 – Sensitive; 1 – Mildly Sensitive; 0 – Resistant.
PIC – Piperacillin; TEC – Teikoplanin; TET – Tetracycline; GEN – Gentamicin; ERY – Erythromycin; KAN – Kanamicin; CIP – Ciprofloxacin; AMP – Ampicillin; VAN – Vancomycin; PE – Penicillin.

duced by the firm bio-Merieux. Identification of microorganisms was performed according to standard bacteriological methods, also using bio-Merieux tests. Antibiotic sensitivity of cultured organisms was assessed using the ATB system antibiogram test for ATB Ur and ATB Strep.

Results

The results of urine analysis are shown in Table 1. The most frequently isolated organisms were colibacilli. *E. coli* was cultured from 11 urine samples. The second most commonly found species was *E. faecalis* which was isolated in 5 cases. In 13 cases the causative etiological factor in UTI was one species of bacteria. In 5 cases, 2 species were involved and in one case three species were present.

Tables 2 and 3 show the antibiotic sensitivities of *E. coli* and *E. faecalis,* the most common causes of UTI. As shown in Table 2, *E. coli* was classified into 7 sensitivity patterns, each representing a single strain, and 2 patterns which were displayed by 2 strains. One of the 11 strains of *E. coli* shown in the table, displayed resistance to 5 antibiotics, 1 strain to 3 antibiotics, 3 strains to 2 antibiotics. All strains were sensitive to norfloxacin. No strain was confirmed as being resistant to amoxicillin/clarulanic acid. Four strains displayed resistance to cefalotin, two to cefotaxime, ciprofloxacin and cotrimoxazole and one to gentamicin, netylmycin, amikacin and ceftazidime.

Cultures of *E. faecalis* were classified into 4 sensitivity patterns. Three patterns were seen in single strains and one pattern was seen in 2 strains (Table 3). As shown in the Table, 2 strains were resistant to 4 antibiotics, two strains to 3 antibiotics and one strain to 2 antibiotics. All strains had the characteristic of resistance to tetracycline and 4 of these were resistant to erythromycin. All strains were sensitive to piperacillin, vancomycin, teikoplanine, ampicillin and penicillin.

P. aeruginosa was isolated from 3 patients and displayed sensitivity to ceftazidine and imipenem. The greatest resistance to antibiotics was seen in the case of *K. pneumoniae* which was isolated from one patient, aged 47, who had undergone resection of the uterus and left kidney. This organism was resistant to amoxicillin/clarulanic acid, cefotaxime, cotrimoxazole, gentamicin, netylmicin and amikacine. It was sensitive only to norfloxacin.

Discussion

The results of the tests performed show that the most frequent etiological factor causing UTI in female patients with

neoplastic diseases of the sex organs was *E. coli*. This agrees with other authors in that *E. coli* is the most commonly observed bacterial species causing UTI [8]. Four strains of *E. coli* displayed resistance to cephalosporins, frequently used drugs in the treatment of UTI. Other authors have also described an increase in the number of species resistant to cephalosporins in cases of UTI [21]. Our results draw attention to the emergence of organisms resistant to ciprofloxacin and cotrimoxazole, drugs many authors list as standard treatments for UTI [22–24]. Also, antibiograms on tested materials showed that 3 strains of *E. faecalis* were resistant to aminoglycosides, antibiotics used in the treatment of UTI [25]. VRE (Vancomycin Resistant Enterococcus) were not observed though these are currently a serious threat owing to high drug resistance in these species. Attention is drawn to the emergence of a strain of *K. pneumoniae,* which is multi-drug resistant, isolated from a patient being treated for cancer of the uterine cervix. Other authors have also written about the high resistance of *K. pneumoniae* [26,27].

The results of our investigation show UTI in four patients with stage I B, four with stage III B and one with stage IV cancer of the uterine cervix. Prasad et al. (1995) showed that advanced cervical cancer may have effects leading to UTI. Authors have described a higher percentage (33.3%) of infections in patients with stage III cervical cancer in comparison to patients with stage II disease (16.7% UTI) [6].

Conclusion

The results of this study show that *E. coli* and *E. faecalis* may generally be isolated from the urine of female patients with neoplastic disease of the genitourinary tract and that these species are therefore the most common causative factor in infection of the urinary tract. Comparison of species' resistance patterns may be used in epidemiological studies in order to discover the source of infections and therefore has a profound significance in the prophylaxis of nosocomial infections.

References:

1. Foxman B: Epidemiology of urinary tract infections: Incidence, morbidity, and economic costs. Am J Med, 2002; 113(Suppl.1): 5S–13S
2. Kampf G, Gastmeier P, Wischnewski N et al: Analysis of risk factors for nosocomial infections. Results from the first national prevalence survey in Germany (NIDEP study, part 1). J Hospital Infect, 1997; 37: 103–12
3. Stapleton A: Urinary tract infections in patients with diabetes. Am J Med, 2002; 113(1A): 80S–84S
4. Foxman B, Somsel P, Tallman P et al: Urinary tract infection among women aged 40 to 65: Behavioral and sexual risk factors. J Clin Epidemiol, 2001; 54: 710–18
5. Bialas I, Bessell EM, Sokal M, Slack R: A prospective study of urinary tract infection during pelvic radiotherapy. Radiother Oncol, 1989; 16: 305–9
6. Prasad KN, Pradhan S, Datta NR: Urinary tract infection in patients of gynecological malignancies undergoing external pelvic radiotherapy. Gynecol Oncol, 1995; 57: 380–82
7. Finkelstein R, Rabino G, Kassis I, Mahamid E: Device-associated, device-day infection rates in an Israeli adult general intensive care unit. J Hosp Infect, 2000; 44: 200–5
8. Gupta K: Addressing antibiotic resistance. Am J Med, 2002; 113: 29S–34S
9. Wong AHM, Wenzel RP, Edmond MB: Epidemiology of bacteriuria caused by vancomycin-resistant enterococci – a retrospective study. Am J Infect Control, 2000; 28: 277–81
10. Bouza E, San-Juan R, Munoz P et al: A European perspective on nosocomial urinary tract infections I. Report on the microbiology workload, etiology and antimicrobial susceptibility (ESGNI-003 study). European Study Group on Nosocomial Infections. Clin Microbiol Infect, 2001; 7: 523–31
11. Laupland KB, Zygun DA, Davies HD et al: Incidence and risk factors for acquiring nosocomial urinary tract infection in the critically ill. J Crit Care, 2002; 17: 50–57
12. Warren JW: Catheter-associated urinary tract infections. Int J Antimicrob Agents, 2001; 17: 299–303
13. Manges AR, Johnson JR, Foxman B et al: Widespread distribution of urinary tract infections caused by a multidrug-resistant Escherichia coli clonal group. N Engl J Med, 2001; 345: 1007–13
14. Karchmer TB, Giannetta ET, Muto CA et al: A randomized crossover study of silver-coated urinary catheters in hospitalized patients. Arch Intern Med, 2000; 160: 3294–98
15. Lai KK, Fontecchio SA: Use of silver-hydrogel urinary catheters on the incidence of catheter-associated urinary tract infections in hospitalized patients. Am J Infect Control, 2002; 30: 221–25
16. Tauchnitz C: Diagnostik und Therapie von Harnwegsinfektionen. Z Gesamte Inn Med, 1992; 47: 404–8
17. Bafna UD, Tasneem RI: Inadvertent bladder injury due to tumour infiltration during radical hysterectomy procedure for cervical cancer: complete healing with postoperative chemotherapy. J Obstet Gynaecol, 2002; 22: 703
18. Fujikawa K, Miyamoto T, Ihara Y et al: High incidence of severe urologic complications following radiotherapy for cervical cancer in Japanese women. Gynecol Oncol, 2001; 80: 21–23
19. Zola P, Ferrero A, Fuso L et al: Different types of hysterectomy in the radio-surgical treatment of early cervical cancer (FIGO Ib-IIa). Eur J Gynaecol Oncol, 2002; 23: 236–42
20. Levenback C, Eifel PJ, Burke TW et al: Hemorrhagic cystitis following radiotherapy for stage Ib cancer of the cervix. Gynecol Oncol, 1994; 55: 206–10
21. Takahashi K, Muratani T, Iihara K et al: Treatment of urinary tract infections caused by strains resistant to fluoroquinolones and cephems. Nishinihon J Urol, 2002; 64: 295–301
22. Johnson JR: Appropriateness of fluoroquinolones for therapy of urinary tract infection. Arch Intern Med, 2003; 163: 1616–17
23. Nicolle LE: Urinary tract infections in long-term-care facilities. Infect Control Hosp Epidemiol, 2001; 22: 167–75
24. Stamm WE: Scientific and clinical challenges in the management of urinary tract infections. Am J Med, 2002; 113(1A): 1S–4S
25. Jones RN: Impact of changing pathogens and antimicrobial susceptibility patterns in the treatment of serious infections in hospitalized patients. Am J Med, 1996; 100(6A): 3S–12S
26. Bedenic B: Selection of Klebsiella pneumoniae mutants with high-level cefotaxime resistance during growth in serum containing therapeutic concentrations of cefotaxime. Chemotherapy, 2002; 48: 10–14
27. Senda K, Arakawa Y, Ichiyama S et al: PCR detection of metallo-beta-lactamase gene (blaIMP) in gram-negative rods resistant to broad-spectrum beta-lactams. J Clin Microbiol, 1996; 34: 2909–13